-59-

CLAIMS

What is claimed is:

5

10

15

20

25

1. A compound of the formula I:

the salts, solvates, and prodrugs thereof, in which;

- a) X¹ is represented by halogen, cyano, C₁-C₆ alkoxy, haloalkoxy, or haloalkyl;
- b) A is represented by a linear alkylene group containing from 2 to 10 carbon atoms, in which up to 6 hydrogen atoms may optionally be replaced by a substituent independently selected from the group consisting of:
 - i. halogen,
 - ii. cyano,
 - iii. hydroxy,
 - iv. (C₁-C₁₂)alkyl, optionally substituted,
 - v. (C₂-C₁₂)alkenyl, optionally substituted,
 - vi. (C₂-C₁₂)alkynyl, optionally substituted,
 - vii. (C₃-C₁₀)cycloalkyl, optionally substituted,
 - viii. (C₃-C₁₀) cycloalkyl(C₁-C₆)alkyl, in which the alkyl and cycloalkyl moieties may each be optionally substituted,
 - ix. $(CH_2)_n$ -SR¹,
 - x. $(CH_2)_n O R^1$,
 - xi. $(CH_2)_n$ -NR¹R²,
 - xii. (CH₂)_n-COOR³ and,
 - xiii. (CH₂)_n-CONR⁴;
- c) X^2 is represented by (C_6-C_{10}) aryl, optionally substituted;
- n, at each occurrence, is independently represented by an integer from 0 to 6;

5

25

30

- e) R¹ and R² are each independently represented by a substituent selected from the group consisting of hydrogen and (C₁-C₆)alkyl, optionally substituted;
- f) R³ is represented by a substituent selected from the group consisting of hydrogen, and (C₁-C₀)alky, optionally substituted, and;
- g) R^4 is represented by a substituent selected from the group consisting of hydrogen, and (C_1-C_6) alkyl, optionally substituted.
- 2. A compound according to claim 1 in which A is represented by ethylene, propylene, butylenes, or pentylene, any of which may be optionally substituted.
- 3. A compound according to claim 1 or 2 in which X¹ is trifluoromethyl or chloro and is located at the 3-position of the phenyl ring.
 - 4. A compound according to claim 1, 2, or 3 in which X² is represented by:

- A compound according to claim 1, 2, 3, or 4 in which A is ethylene or propylene and is substituted with at least one substituent represented by (CH₂)_n-O-R¹ or (C₁-C₆)alkyl.
 - 6. A compound according to claim 1 selected from the group consisting of:
 - a. 4,4'-[(2S,3S)-butane-2,3-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile])
 - b. 4,4'-[(2R,3R)-butane-2,3-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
 - c. 4,4'-[but-1-ene-3,4-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

-61-

- d. 4,4'-[pentane-1,2-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
- e. 4,4'-[(3-methoxypropane-1,2-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

5

f. 4,4'-[(3-ethoxypropane-1,2-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

10

- g. 4,4'-[[3-(isopropylamino)propane-1,2-diyl]bis[2-(trifluoromethyl)benzonitrile];
- h. 4,4'-[(6-methylhexane-1,2-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

15

- i. 4,4'-[octane-1,2-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
- j. 4-[1-(4-Cyano-3-trifluoromethyl-phenoxymethyl)-2,2-dimethyl-cyclopropoxy]-2-trifluoromethyl-benzonitrile;

20

- k. 4,4'-[Propane-1,3-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
- 4,4'-[(2-methylpropane-1,3-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

25

- m. 4,4'-[butane-1,3-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
- n. 4-({(3R)-3-[4-cyano-3-(trifluoromethyl)phenoxy]butyl}oxy)-2-(trifluoromethyl)benzonitrile;

30

- o. 4-({(3S)-3-[4-cyano-3-(trifluoromethyl)phenoxy]butyl}oxy)-2-(trifluoromethyl)benzonitrile;
- p. 4-{3-[4-cyano-3-(trifluoromethyl)phenoxy]-1,2-dimethylpropoxy}-2-(trifluoromethyl)benzonitrile;

35

q. 4,4'-[hex-1-ene-4,6-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];

	r. 4,4'-[(3-methylbutane-1,3-diyl)bis(oxy)]bis[2- (trifluoromethyl)benzonitrile];
5	s. 4-{[3-(4-cyanophenoxy)-2-ethylhexyl]oxy}bis[2-(trifluoromethyl)benzonitrile];
10	t. 4,4'-[(2S,4S)-pentane-2,4-diylbis(oxy)]bis[2- (trifluoromethyl)benzonitrile];
	u. 4,4'-[heptane-1,4-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
15	v. 4,4'-[hexane-2,5-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
	w. 4,4'-[(2S,5S)-hexane-2,5-diylbis(oxy)]bis[2- (trifluoromethyl)benzonitrile];
20	x. 4-({5-[4-cyano-2-(trifluoromethyl)phenoxy]pentyl}oxy)-2(trifluoromethyl)benzonitrile;
	y. 4,4'-[hexane-1,5-diylbis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
25	z. 4,4'-[(3-methylpentane-1,5-diyl)bis(oxy)]bis[2-(trifluoromethyl)benzonitrile];
25	aa. 4-(1-methoxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl- benzonitrile;
30	bb. 4-(1-hydroxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl-benzonitrile;
	cc. (1R)-4-(1-hydroxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl- benzonitrile;
35	dd. (1R)-4-(1-methoxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl- benzonitrile;

	ee. (1S)-4-(1-methoxymethyl-2-phenoxy-ethoxy)-2-trifluoromethyl- benzonitrile;
5	ff. 2-chloro-4-(2-methoxy-1-phenoxymethyl-ethoxy)-benzonitrile;
	gg. 2-chloro-4-(1-phenoxymethyl-butoxy)-benzonitrile;
10	hh. 2-chloro-4-(1-phenoxymethyl-propoxy)-benzonitrile;
	ii. 2-chloro-4-(1-phenoxymethyl-butoxy)-benzonitrile;
15 .	jj. 2-chloro-4-[1-(4-methoxy-phenoxymethyl-propoxy)-benzonitrile;
	kk. 2-chloro-4-[1-(2-methoxy-phenoxymethyl-propoxy)-benzonitrile;
	II. 2-chloro-4-[1-methyl-phenoxy-ethoxy)-benzonitrile;
20	mm. 4-[4-(4-cyano-3-trifluoromethyl-phenoxy)- 2-hydroxy-butyloxy]-2-trifluoromethyl-benzonitrile;
	nn. 4-[3-(4-cyano-3-trifluoromethyl-phenoxy)- 2-cyclohexyl-propyloxy] 2-trifluoromethyl-benzonitrile;
25	oo. 4-[3-(4-cyano-3-trifluoromethyl-phenoxy)- 2-cyclohexyl-propyloxy] 2-trifluoromethyl-benzonitrile;
30	pp. 4-[3-(4-cyano-3-trifluoromethyl-phenoxy)- 2-chloro-propyloxy]-2-trifluoromethyl-benzonitrile;
	qq. 4-[8-(4-cyano-3-trifluoromethyl-phenoxy)- 2-chloro-4-hydroxy-octyloxy]-2-trifluoromethyl-benzonitrile;
35	rr. 4-[10-(4-cyano-3-trifluoromethyl-phenoxy)- 2-methylcyclopentyl-octyloxy]-2-trifluoromethyl-benzonitrile:

- ss. 4-[10-(4-cyano-3-trifluoromethyl-phenoxy)- decyloxy]-2-trifluoromethyl-benzonitrile;
- tt. 4-[7-(4-cyano-3-trifluoromethyl-phenoxy)-2-cyano-4-methyl-6-hydroxy-heptyloxy]-2-trifluoromethyl-benzonitrile;
- uu. 4-(3-(3-hydroxy-4-fluoro-phenoxy)-propoxy)-2-trifluoromethylbenzonitrile;
- vv. 4-(2-cyano-4-dimethylamino-8-phenoxy-octyloxy)-2-trifluoromethylbenzonitrile;

5

10

15

20

30

- ww. 4-(2-dimethylamino-2-(4-cyano-phenoxy)-ethyloxy)-2-trifluoromethyl-benzonitrile;
- xx. 4-(1-cyclopentyloxymethyl-3-(4-hydroxy-phenoxy)-propoxy)-2-trifluoromethyl-benzonitrile; and
- yy. 4-(2-methyl-4-dimethylamino-8-phenoxy-octyloxy)-2-trifluoromethyl-benzonitrile.
- 7. Use of a compound according to any one of claims 1-6 as a medicine.
- 8. Use of a compound according to any one of claims 1-6 in the manufacture of a medicament for inhibiting activation of the androgen receptor.
 - 9. Use of a compound according to any one of claims 1-6 in the manufacture of a medicament for alleviating a condition selected from the group consisting of hormone dependent cancers, benign hyperplasia of the prostate, acne, hirsutism, excess sebum, alopecia, premenstrual syndrome, lung cancer, precocious puberty, osteoporosis, hypogonadism, age-related decrease in muscle mass, and anemia.

-65-

- A pharmaceutical composition comprising a compound according to any one of claims 1-6 in admixture with one or more pharmaceutically acceptable excipients.
- A topical pharmaceutical formulation comprising a compound according to any one of claims 1-6 in admixture with or more pharmaceutically acceptable excipients suitable for dermal application.
- 12. An article of manufacture comprising a compound according to any one of claims 1-6 packaged for retail distribution, which advises a consumer how to utilize the compound to alleviate a condition selected from the group consisting of acne, alopecia, and oily skin.